Docket No.: D0590.70011US00

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**



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| Applicant: | Plaetinck et al. |
| Serial No.: | 10/057108 |
| Confirmation No.: | 1549 |
| Filed: | January 25, 2002 |
| For: | CHARACTERISATION OF GENE FUNCTION USING DOUBLE STRANDED RNA INHIBITION |
| Examiner: | Joseph T. Woitach |
| Art Unit: | 1632 |

The undersigned hereby certifies that this document is being transmitted via facsimile to the United States Patent and Trademark Office in accordance with 37 C.F.R. §1.6(d) to the attention of MS 313(c), Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, at facsimile number 571-273-0025, on the date shown below.

Dated: 5/10/06 Signature: Jane M Watson (Jane M. Watson)

**MAIL STOP 313(c)**
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

STATEMENT FILED PURSUANT TO THE DUTY OF DISCLOSURE UNDER 37 CFR §§1.56, 1.97 AND 1.98

Sir:

Pursuant to the duty of disclosure under 37 C.F.R. §§1.56, 1.97 and 1.98, the Applicant requests consideration of this Information Disclosure Statement.

PART I: Compliance with 37 C.F.R. §1.97

This Information Disclosure Statement has been filed before the mailing of a first Office action after the filing of a request for continued examination under 37 C.F.R. §1.114.

No fee or certification is required.

PART III: Information Cited

The Applicant hereby makes of record in the above-identified application the information listed on the attached form PTO-1449 (modified PTO/SB/08). The order of presentation of the references should not be construed as an indication of the importance of the references.

The Applicant would like to bring to the Examiner's attention the following other information, whose relevance is discussed in Part IV below: The reference cited was previously cited in an Information Disclosure Statement.

PART IV: Explanation of Non-English Language References and Remarks Concerning Other Information Cited

The following is a concise explanation of the relevance of each non-English language reference listed on the attached form PTO-1449 (modified PTO/SB/08):

The following are remarks concerning the other information cited: The previously filed PTO-1449 accompanying the above-referenced Information Disclosure Statement inadvertently listed the 1998 East Coast Worm Meeting Abstract with the date June 27, 2002 in parentheses. This abstract is cited again herewith to correct this typographical error in the PTO-1449 listing. The date of availability of this reference was May 12, 1998.

PART V: Remarks

Documents cited anywhere in the Information Disclosure Statement are enclosed unless otherwise indicated. It is respectfully requested that:

1. The Examiner consider completely the cited information, along with any other information, in reaching a determination concerning the patentability of the present claims;

2. The enclosed form PTO-1449 (modified PTO/SB/08) be signed by the Examiner to evidence that the cited information has been fully considered by the Patent and Trademark Office during the examination of this application;

3. The citations for the information be printed on any patent which issues from this application.

By submitting this Information Disclosure Statement, the Applicant makes no representation that a search has been performed, of the extent of any search performed, or that more relevant information does not exist.

By submitting this Information Disclosure Statement, the Applicant makes no representation that the information cited in the Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. §1.56(b).

By submitting this Information Disclosure Statement, the Applicant makes no representation that the information cited in the Statement is, or is considered to be, in fact, prior art as defined by 35 U.S.C. §102.

Notwithstanding any statements by the Applicant, the Examiner is urged to form his or her own conclusion regarding the relevance of the cited information.

An early and favorable action is hereby requested.

Respectfully submitted,

By: 

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Docket No.: D0590.70011US00
Date: May 10, 2006
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| FORM PTO-1449/A and B (Modified) | APPLICATION NO.: 10/057,108 | DOCKET NO.: D0590.70[illegible]VSC |
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| **INFORMATION DISCLOSURE STATEMENT BY APPLICANT** | FILING DATE: January 25, 2002 | Confirmation No.: 1549 |
| | APPLICANT: Plaetinck et al. | |
| Sheet 1 of 1 | GROUP ART UNIT: 1632 | EXAMINER: Joseph T. Woitach |

**U.S. PATENT DOCUMENTS**

| Examiner's Initials# | Cite No. | U.S. Patent Document Number | U.S. Patent Document Kind Code | Name of Patentee or Applicant of Cited Document | Date of Publication or of issue of Cited Document MM-DD-YYY |
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**FOREIGN PATENT DOCUMENTS**

| Examiner's Initials# | Cite No. | Foreign Patent Document Office/ Country | Foreign Patent Document Number | Foreign Patent Document Kind Code | Name of Patentee or Applicant of Cited Document (not necessary) | Date of Publication of Cited Document MM-DD-YYYY | Translation (Y/N) |
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**OTHER ART — NON PATENT LITERATURE DOCUMENTS**

| Examiner's Initials# | Cite No | Include name of the author (in CAPITAL LETTERS) title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, relevant page(s), volume-issue number(s), publisher, city and/or country where published. | Translation (Y/N) |
|---|---|---|---|
| | | TIMMONS and FIRE, *East Coast Worm Meeting Abstract 180* (May 12, 1998) | |
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| EXAMINER | DATE CONSIDERED |
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#EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

1024578.1

1998 East Coast Worm Meeting abstract 186



# CREATION OF HYPOMORPHIC PSEUDO-MUTANTS VIA BACTERIAL-MEDIATED RNAi.

## Lisa Timmons, Andrew Fire

Carnegie Institution of Washington, Department of Embryology, 115 West University Parkway, Baltimore, Maryland 21210

In an effort to understand the both the mechanism underlying RNAi phenomena and to understand the "normal" purpose for this phenomenon in C. elegans, we have focused on some interesting features of RNAi technology which we believe are noteworthy: (1) the double-stranded RNA used to mediate RNAi need not be injected into the germline in order for the F1 progeny to be affected. (2) the dsRNA, or some effect mediated by the dsRNA, appears to spread from the site of injection throughout the injected animal. These two features are made evident when dsRNA is injected into the body cavity or gut of animals (Fire et al., 1998). Cells from an animal so injected which are far removed from the injection site can be affected by dsRNA, and F1 progeny from such an animal often exhibit the RNAi affect. For example, if dsRNA composed of GFP sequences is injected into the body cavity of an adult transgenic GFP animal, GFP expression is often reduced not only in F1 progeny, but in some adult somatic cells of the injected animal. We wondered if the "spreading" effect of dsRNA would be observed if dsRNA was delivered to the gut via feeding the worms with bacteria that express dsRNA.

Bacteria expressing GFP or unc-22 dsRNA were fed to myo3::GFP worms on standard NGM plates. myo3::GFP worms consistently express a high level of GFP in muscle from shortly before hatching through adult. A reduction in muscle cell GFP expression was observed in animals fed bacteria expressing double-stranded GFP RNA. Adult animals appeared mosaic for GFP expression: some adults had an overall reduction in the amount of GFP, a few animals appeared null for GFP expression. All animals regained activity in the next generation when transferred to standard bacteria (without the dsRNA). Animals grown on bacteria expressing double-stranded unc-22 RNA showed no loss of GFP expression. Instead, 90% of these animals exhibited a weak twitching phenotype.

In conclusion, we observe specific RNAi effects in worms that have injested dsRNA. Our results provide evidence of a mechanism by which dsRNA can be taken up by the gut and spread through the animal. In addition, our observations lead us to speculate that worms have a natural defense against dsRNA viruses, and that RNAi technology is made possible by utilizing at least a part of the defense mechanism pathway. In summary, be careful what you eat.

Fire, A., Xu, S., Montgomery, M., Kostas, S., Driver, S., and Mello, C. Nature 391:806, 1998.